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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/522,727 | 03/10/2000 | Wayne A Marasco | 47577-C | 5205 |

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| EXAMINER | |
|---|---|
| OUSPENSKI, ILIA I | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

DATE MAILED: 07/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/522,727 | MARASCO ET AL. | |
| | Examiner | Art Unit | |
| | ILIA OUSPENSKI | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *13 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,4 and 7-24* is/are pending in the application.

4a) Of the above claim(s) *1,4,7-17,20,21 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,19,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.



S.O.O

## DETAILED ACTION

1. Applicant's amendment, filed 05/13/2005, is acknowledged.

Claims 2, 3, 5, and 6 have been cancelled previously.

Claims 1, 4, and 7 – 24 are pending.

Claims 1, 4, 7 – 17, 20, 21, and 24 have been previously withdrawn from consideration by the Examiner as being drawn to nonelected inventions.

*Claims 18, 19, 22, and 23, as they read on the elected species of the originally presented invention, are under consideration in the instant application.*

2. This Office Action will be in response to applicant's arguments, filed 05/13/2005.

The rejections of record can be found in the previous Office Action, mailed 02/07/2005.

The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

**3. Claim rejection under 35 USC103(a):**

Claims 18, 19, 22, and 23 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Marasco et al. (WO 94/02610, of record, see entire document) in view of Marasco et al. (US Patent No. 6,143,520; see entire document).

Applicant's arguments have been fully considered but have not been found convincing.

Applicant argues that each reference individually does not teach the instantly claimed limitations, and that the combination of references allegedly does not provide a motivation for using an IRES sequence in the claimed method. In particular, Applicant points that the present invention teaches the advantages of using an IRES sequence to solve specific problem of a setting in which forced expression is desirable, specifically silencing.

This is not found persuasive because the references, when combined, explicitly teach all of the claimed limitations. The motivation for using the IRES sequences in the claimed method is explicitly provided by the '520 Patent, which teaches, for example, that it is "desirable to have vectors and/or methods that would reduce the ability of selection pressure to silence, or otherwise select against [exogenous] genes," and that applying these methods specifically to intracellular antibodies can enhance the effectiveness of their use (column 1 lines 52 – 63).

Therefore, the rejection of record is maintained for the reasons of record. The rejection of record is reiterated herein for Applicant's convenience.

Claims 18, 19, 22, and 23 rejected under **35 U.S.C. 103(a)** as being unpatentable over Marasco et al. (WO 94/02610, of record, see entire document) in view of Marasco et al. (US Patent No. 6,143,520; see entire document).

The applied references have a common Inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the

application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

As discusses in previous Office Actions, WO 94/02610 teaches methods of intracellular binding of target molecules by expressing a gene encoding a single chain antibody in a cell (see entire document, e.g., Abstract and "Summary of the Invention" on pages 4-5). WO 94/02610 teaches that this method can be applied to disrupt a function that is undesirable at a particular time, including the recognition of antigens by the immune system at times when an immune response is undesired, as during transplantation of organs (see entire document, but especially e.g. page 16 lines 1-16). WO 94/02610 further teaches that said single chain antibody can be a Fab fragment (e.g. page 24 last paragraph, page 44 last paragraph, or claim 47), and that the preferred vector for expression of the antibody is a retroviral vector (e.g. pages 46 – 47 bridging paragraph). WO 94/02610 reviews a need for such methods at the time the invention was made (page 3 line 22 – page 4 line 5).

WO 94/02610 does not teach the use of an internal ribosome entry site (IRES) for expression of the antibody, and does not specifically exemplify the use of lentivirus vectors.

US Patent No. 6,143,520 teaches and claims lentivirus vectors containing IRES for expression of genes of interest (see entire document, in particular, e.g. claim 1), such as those encoding intracellular antibodies (intrabodies) (e.g. column 3 first paragraph). US Patent No. 6,143,520 further discloses numerous advantages of using IRES in general, an in combination with a lentivirus vector in particular, over other expression systems, and especially as it applies to expression of intrabodies (see entire document, in particular, e.g. Results at columns 8 – 9).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of US Patent No. 6,143,520 to those of WO 94/02610 to arrive at the claimed method. One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because of the need for such methods, as reviewed by WO 94/02610, and the advantages of using IRES and lentivirus vectors for expression of intrabodies, as taught by US Patent No. 6,143,520. One of ordinary skill in the art would have had a

reasonable expectation of success in producing the claimed invention, as demonstrated by the Examples in US Patent No. 6,143,520.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

## *4. Conclusion: no claim is allowed.*

5. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ILIA OUSPENSKI
Patent Examiner
Art Unit 1644

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600

June 24, 2005

6/17/05